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the level of nicotine reduction that would be "acceptable to the smoker" is separate from the problem of determining what taste difference would be tolerated. Had Wakeham believed that nicotine is essential only for taste, only the second question would have been relevent. Instead, he recognized that a reduction in nicotine would not be acceptable to smokers for the additional reasons he had already spelled out: that nicotine produces mood-altering reactions that smokers seek. The plain language of the document thus fails to substantiate Philip Morris' claim that Wakeham believed that nicotine is essential only for taste. As in many other tobacco company documents, nicotine's role in taste, if it is mentioned at all, is seen as secondary to its pharmacological role. *See* Jurisdictional Analysis, 60 FR 41772–41778.

5. Philip Morris argues that some of the statements cited by FDA were only Philip Morris researchers' "premises" and "working hypotheses" or even the hypotheses of outside researchers. According to Philip Morris, these statements are not "facts" or conclusions based on data and are therefore irrelevant to intended use.

FDA disagrees that these consistent statements of Philip Morris researchers that people smoke to obtain the pharmacological effects of nicotine are irrelevant to Philip Morris' intent in manufacturing and marketing cigarettes. In establishing the intended use of Philip Morris' tobacco products, the premises, hypotheses, and beliefs of the scientists whose job within the company is to understand the motives for smoking, and who regularly communicate those views to company executives, are highly relevant. Philip Morris and other tobacco companies contend that cigarettes are labeled for "pleasure," not pharmacological effects, and that nicotine is present in cigarettes only for flavor. On this basis, the company argues that cigarettes are not intended as drugs or devices. Nowhere,

however, in the publicly available Philip Morris documents, or in the documents produced by Philip Morris in this proceeding, do their scientists put forward a premise or hypothesis that people smoke primarily for nicotine's flavor and/or any other nonpharmacological motive—much less communicate such a view to company executives. The evidence in the administrative record demonstrates, instead, that during the entire period covered by those documents, Philip Morris scientists were communicating to their superiors their scientific opinion that nicotine's pharmacological effects are the primary motivator of smoking behavior.

6. Philip Morris also argues that its researchers' "hypotheses" were not ultimately supported by the results of their research.

FDA disagrees that the documents show that the major premises of Philip Morris scientists concerning the role of nicotine in tobacco use were disproven. These premises center on the scientists' often stated belief that cigarette smoking is reinforced by the pharmacological effects of nicotine on the brain. In fact, this premise continued to be repeated and even strengthened over the period of research reflected in the documents. For example, the major premise of a 1974 research report is that "the smoking habit is maintained by the reinforcing effects of the pharmacologically active components of smoke. A corollary to this premise is that the smoker will regulate his smoke intake so as to achieve his habitual quota of the pharmacological action."[841]

Philip Morris attempts to use this research report in support of its claim that Philip Morris scientists failed to find support for their beliefs that people smoke to obtain the

[841] Philip Morris Research Center, *Behavioral Research Annual Report, Part II* (Nov. 1, 1974) (approved by Osdene TS), in 141 Cong. Rec. H7658, H7660 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

pharmacological effects of nicotine. According to Philip Morris, this report refuted the compensation theory.[842] Philip Morris' claim that its researchers refuted their major premises fails on two grounds. First, the document shows that Philip Morris researchers considered the compensation theory to be at most a "corollary" of their major premise that smoking is maintained by the reinforcing effects of nicotine. Philip Morris makes no attempt to show that the major premise was disproven. Nor could it. Philip Morris conducted one of the earliest definitive studies on nicotine's reinforcing effects in the early 1980's, well before similar research had been published by outside scientists. As William Dunn told T.S. Osdene, Philip Morris' director of research, the company's research made "it quite clear that nicotine can function as a positive reinforcer for rats."[843] As described in section II.A.3.c.i., above, the ability of a substance to function as a "positive reinforcer" in animals is one of the most telling pieces of evidence that the substance will be addictive in humans.

Second, both the 1974 and subsequent research reports (through and including the last available report in 1980) show that Philip Morris continued to believe in, and test, the compensation theory, using ever more sophisticated and precise methods. Philip Morris relies on a statement from the 1974 report in which the researchers note that previous attempts to show compensation by analyzing the number and amount of cigarettes smoked had shown positive trends but not convincing evidence that the smoker regulates intake of

[842] "Compensation," as described in section II.A.7.i., above, describes the behavior of smokers who are given cigarettes with more or less nicotine than their usual brands. Data, including tobacco industry data, show that smokers "compensate" by altering their smoking behavior (e.g., by smoking more cigarettes or smoking each cigarette more intensely) to obtain their customary nicotine intake.

[843] Dunn WL (Philip Morris Inc.), *Plans and Objectives–1981* (Nov. 26, 1980), in 141 Cong. Rec. H7681-7682 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

nicotine. Philip Morris omits subsequent statements demonstrating that the researchers have not "refuted" the compensation theory, but have merely decided to take a new approach to establishing compensation. Following the statement quoted by Philip Morris, the researchers state that they "question whether the indices of intake which have been investigated to date are, in fact, the appropriate indices to be measuring."[844] Instead, they believe that new evidence suggests that compensation may be accomplished through the inhalation patterns of smokers:

> [O]bservations [concerning differences in how smoke is inhaled from smoker to smoker] have made us aware of a heretofore unnoticed mechanism that has the potential of affording the smoker a wide latitude of control over the amount of smoke he brings into contact with the absorption sites.[845]

The researchers go on to describe a new series of experiments designed "to systematically observe the inhalation patterns of smokers" and thereby determine whether compensation for nicotine is occurring.[846] The researchers also developed, three years later, a new theoretical model to explain their inability up to that point to demonstrate compensation. Under this theory, some smoking is triggered by "deficits or surfeits of nicotine (or some unknown smoke components)" and some by external stimuli:

> The adoption of this point of view by members of the staff will lead us to recognize that apparent failures of [the] nicotine compensation model may not in fact be failures at all and that *nicotine compensation is a real phenomenon which is masked by the fact that smokers smoke many cigarettes out of habit rather than need.*[847]

[844] Philip Morris Research Center, *Behavioral Research Annual Report, Part II* (Nov. 1, 1994), in 141 Cong. Rec. H7658, 7660 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

[845] *Id.*

[846] *Id.*

[847] Dunn WL (Philip Morris Inc.), *Behavioral Research Accomplishments–1977* (Dec. 19, 1977), in 141 Cong. Rec. H7666-7667 (daily ed. Jul. 25, 1995) (emphasis added). *See* AR (Vol. 14 Ref. 175a).

The Philip Morris research reports demonstrate that Philip Morris continued to attempt to measure inhalation patterns throughout the period covered by the reports, and that the researchers continued to believe, and sometimes showed, that smokers compensate for nicotine.[848]

Finally, Philip Morris cites a small number of minor studies in the Philip Morris research documents in which the researchers did not find discernible effects due to smoking; it claims that these show that Philip Morris failed to find support for the belief that nicotine's pharmacological effects motivate smoking. The apparent failure of a small fraction of its studies to demonstrate particular pharmacological effects from nicotine cannot obscure what is evident from a fair reading of the publicly available research reports: the company's research on nicotine demonstrated that nicotine had many significant pharmacological effects on smokers. The record also shows that, through the period covered by the reports, Philip Morris' emphasis on the pharmacological motivations for smoking increased and its research on the pharmacological effects of nicotine grew in size and sophistication. By the end of that period, Philip Morris had successfully established that nicotine is a positive reinforcer in rats, that it produces psychoactive effects like other drugs of abuse, that it produces tolerance, and that it acts

[848] *See, e.g.,* Letter from Dunn WL to Schachter S (Sep. 8, 1975) (Philip Morris expects inhalation patterns "to be dose-regulating mechanisms of remarkable precision and sensitivity"), in 141 Cong. Rec. H7662 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

Dunn WL (Philip Morris Inc.), *Behavioral Research Accomplishments–1977* (Dec. 19, 1977) ("We have . . . [s]hown that we can distinguish between [nicotine] regulator and nonregulator smokers and that after being deprived, the regulators do indeed try to make up for lost intake"), in 141 Cong. Rec. H7666 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

Dunn WL (Philip Morris Inc.), *Plans and Objectives–1981* (Nov. 26, 1980), in 141 Cong. Rec. H7681, H7683 (daily ed. Jul. 25, 1995). *See* AR (Vol. 14 Ref. 175a).

centrally in the brain. These are the standard animal tests performed by pharmaceutical companies and public health organizations to establish that a substance is addictive. At this time, Philip Morris was also engaged in a broad-based study of the effects of smoking and nicotine on *human* brain wave patterns to "identify as far as possible the neural elements which mediate cigarette smoking's reinforcing actions."[849] The record thus contradicts Philip Morris' claim that its research failed to bear out the premise that people smoke to obtain nicotine.

7. Philip Morris argues that FDA has mischaracterized statements of Philip Morris officials in several company documents related to the addictive effects of nicotine and cigarettes. FDA has reviewed the statements and concluded that it has not mischaracterized the statements that it relied on.

First, in the Jurisdictional Analysis, 60 FR 41607–41608, FDA cited a Philip Morris study on a smoking cessation campaign in Greenfield, Iowa, in 1969 as evidence that Philip Morris researchers recognized that smoking cessation produces a withdrawal syndrome. Philip Morris claims that its study did not conclude that nicotine is "addictive" and that the study showed only that former smokers experienced "transient . . . common behavioral mannerisms such as eating more, tapping their fingers, twiddling their thumbs, biting their lips, chewing on matches, or feeling ill-tempered."[850] Philip Morris also argues that this study was published more than 20 years ago and therefore is not "new" evidence.

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[849] *Id.* at H7681.

[850] Philip Morris Inc., Comment (Jan. 2, 1996), at 17. *See* AR (Vol. 519 Ref. 105).

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FDA believes that the Philip Morris study on the Iowa "cold turkey" campaign provides solid evidence that Philip Morris knows that abstinence from smoking produces a significant, long-term withdrawal syndrome. As discussed in section II.A.3., above, withdrawal is recognized as one of the characteristic features of drug dependence. Contrary to the comment's claim that the study revealed only mild and "transient" symptoms, the study author, a Philip Morris researcher, summarizes the symptoms of those who quit smoking this way:

> Even after *eight months* quitters were apt to report having neurotic symptoms, such as feeling depressed, being restless and tense, being ill-tempered, having loss of energy, being apt to doze off, etc. They were further troubled by constipation and weight gains which averaged about 5 lbs. per quitter.[851]

The researcher later reports on the worsening of health symptoms among the quitters, observing that their "list of complaints is long and impressive."[852] The author encapsulates the quitters' experience as follows:

> This is not the happy picture painted by the Cancer Society's anti-smoking commercial which shows an exuberant couple leaping in the air and kicking their heels with joy because they've kicked the habit. A more appropriate commercial would show *a restless, nervous, constipated husband bickering viciously with his bitchy wife who is nagging him about his slothful behavior and growing waistline.*[853]

Accordingly, this study provides evidence that Philip Morris knows that smokers suffer significant, long-term withdrawal symptoms, a characteristic feature of addictive

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[851] Ryan FJ (Philip Morris Inc.), *Bird-1: A Study of the Quit-Smoking Campaign in Greenfield, Iowa, in Conjunction with Movie, Cold Turkey* (Mar. 1971), at 1. (emphasis added). *See* AR (Vol. 390 Ref. 6394).

[852] *Id.* at 31.

[853] *Id.* at 33 (emphasis added).

substances. There is no support for Philip Morris' contention that the withdrawal symptoms reported in this study are not comparable to withdrawal symptoms from other drugs that produce physical dependence. The withdrawal symptoms reported by Philip Morris include many of the same changes in mood, behavior, and physical functioning identified as evidence of a withdrawal syndrome for all drugs that produce physical dependence. They are the same symptoms that have been recognized by the Surgeon General and other public health organizations as evidence that nicotine produces a withdrawal syndrome and physical dependence.[854]

Finally, Philip Morris' claim that this study was published 20 years ago is misleading. The material quoted in the Jurisdictional Analysis and here comes principally from an internal Philip Morris study report that was not published.[855] Another version of the study was published, in which the quoted material was omitted.[856]

Philip Morris also argues that FDA "deliberately mischaracterize[d]" another Philip Morris document in which Philip Morris acknowledges both nicotine dependence and a withdrawal syndrome from cigarette deprivation. FDA notes that Philip Morris challenges only the use of the statement to show that Philip Morris acknowledges withdrawal; Philip Morris makes no claim that this statement does not acknowledge nicotine dependence.

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[854] Surgeon General's Report, 1988, at 198-221. *See* AR (Vol. 129 Ref. 1592).

American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed. (Washington DC: American Psychiatric Association, 1994), at 244. *See* AR (Vol. 5 Ref. 46-1).

[855] Ryan FJ (Philip Morris Inc.), *Bird-1: A Study of the Quit-Smoking Campaign in Greenfield, Iowa, in Conjunction with Movie, Cold Turkey* (Mar. 1971). *See* AR (Vol. 21 Ref. 207).

[856] Ryan FJ (Philip Morris Inc.), Cold turkey in Greenfield, Iowa: a follow-up study, in *Smoking Behavior: Motives and Incentives,* ed. Dunn WL (Washington DC: VH Winston & Sons, 1973). *See* AR (Vol. 8 Ref. 105).

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The document is a report from W. L. Dunn to T. S. Osdene, vice president for research and development, entitled, "Plans and Objectives–1980." In describing the company's "Experimental Psychology Program," the report states that the first objective of the program is to "gain better understanding of the role of nicotine in smoking." The report describes one of its approaches to this objective as follows:

> Identification of two smoking population subgroups, one of which has greater nicotine needs than the other. We have described these people in the past as compensators and noncompensators, and attempted to define them by their consumption changes when nicotine deliveries were moderately shifted. However, we've had no great success in the identification to date. Now we may have two extra tools to use: Commercial PM cigarettes of ultra low tar and nicotine, and salivary nicotine concentrations. Others, principally at Columbia University, have suggested that shifts to ultra low nicotine cigarettes produce the same type of psychological stress behaviors as quitting. *We therefore propose a shift study in which smokers are shifted to an ultra low brand, and the key dependent variable becomes the presence or absence of the withdrawal syndrome. Those who show evidence of nicotine dependence and those who do not can then be used to test our hypotheses on the relationship of salivary concentration to smoking behavior.*[857]

Philip Morris claims that this statement contains no acknowledgment of a cigarette withdrawal syndrome, because the Philip Morris researchers: (1) found no support for their hypothesis that people compensate for changes in nicotine yield; (2) were merely testing hypotheses proposed by outside researchers; and (3) were referring to psychological stress behaviors, not physiological symptoms when they spoke of withdrawal.

The full text of this statement fails to support Philip Morris' strained construction. The obvious purpose of the statement is to explain that the researchers intended to try a

[857] Dunn WL (Philip Morris Inc.), *Plans and Objectives–1980* (Jan. 7, 1980), in 141 Cong. Rec. H7670, H7672 (daily ed. Jul. 25, 1995) (emphasis added). *See* AR (Vol. 14 Ref. 175a).

new approach to identifying "compensators" and "noncompensators," relying on evidence of withdrawal/dependence. The researchers are clear that withdrawal is an established syndrome they will use to identify compensators and noncompensators, not the reverse. The only outside hypothesis mentioned in the statement is the notion that switching to ultra-low nicotine cigarettes can be used to induce the same stress behaviors as quitting. The more fundamental notion that quitting produces a withdrawal syndrome is not an outsider's hypothesis but a clearly accepted premise of the entire approach. Nothing in the statement suggests that the researchers intend to test an "hypothesis" that quitting produces withdrawal; they intend to use this accepted fact to search for compensators and noncompensators. Finally, there is no evidence in the document to support Philip Morris' assertion that the Philip Morris researchers were referring to psychological stress behaviors, not physiological symptoms.

Philip Morris also contends that FDA inappropriately characterized a Philip Morris memo, which FDA briefly cited in a footnote to the Jurisdictional Analysis, as indicating that people smoke to avoid "withdrawal." According to Philip Morris, the memo merely placed cigarettes in the same category as alcohol, tea, coffee, chewing gum, overeating, and sex.

Philip Morris' characterization focuses on the introduction of the memo, while ignoring its central purpose. The actual purpose of the memo is to propose to study the question of why people continue to smoke despite "compelling pressures upon the smoker to discontinue the behavior" and to "document the penalties imposed by discontinuation of